

# United States Patent [19]

Gillonier et al.

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[54] **PROCESS FOR PREPARING AN AQUEOUS SOLUTION OF AN ALKALI METAL SALT OF METHIONINE**

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### Related U.S. Application Data

[63] Continuation of Ser. No. 936,393, Dec. 1, 1986, abandoned.

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[52] U.S. Cl. .... **562/559**

[58] Field of Search ..... **562/559**

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### [57] ABSTRACT

An aqueous solution of an alkali metal salt of methionine, which can be used as an additive in feedstuffs, is made by hydrolysis of methionine amide with an alkali metal hydroxide.

**2 Claims, No Drawings**

**PROCESS FOR PREPARING AN AQUEOUS  
SOLUTION OF AN ALKALI METAL SALT OF  
METHIONINE**

This is a continuation of application Ser. No. 936,393, filed Dec. 1, 1986, now abandoned.

The present invention relates to preparing an aqueous solution of an alkali metal salt of methionine which can be used as an additive in feedstuffs for livestock.

Methionine, which is an essential amino acid, is used at low doses, generally less than 1%, as an additive in feedstuffs. It is important to be able to produce a homogeneous dispersion of methionine in the feed and to be able to proportion the methionine accurately.

The use of methionine in crystallized solid form has disadvantages which make it difficult to handle and proportion.

The use of solutions enables a homogeneous dispersion to be produced at concentrations which can be readily monitored.

Since methionine is only slightly soluble in water, it cannot be used as such in aqueous solution on account of the considerable volume which would have to be handled. However, alkali metal salts of methionine have greater solubility in water, and can be used in sufficiently concentrated solutions to achieve the objective sought.

Solutions of alkali metal methioninate, especially sodium methioninate, can be prepared by dissolving methionine in an aqueous solution of an alkali metal hydroxide. However, this procedure is not economically advantageous since it is necessary to isolate the methionine beforehand, before dissolving it in a suitable medium.

It is also known, from French Patent Application Nos. 2,499,560, 2,499,563, 2,499,564, 2,499,565 and 2,499,566, to prepare aqueous solutions of sodium methioninate by saponification of 5-( $\beta$ -methylmercaptoethyl)hydantoin with an excess of sodium carbonate and/or sodium carbonate and/or lime. However, during the saponification, substantial amounts of sodium hydroxide and/or calcium carbonate are formed, and have to be removed by suitable treatments (concentration, precipitation, filtration, etc).

According to French Patent No. 2,372,797, it is known to prepare methionine from the corresponding aminonitrile by the action of hydroxide ions in the presence of a ketone, the reaction proceeding via the intermediate aminoamide. According to this process, the hydrolysis is performed in an aqueous medium containing an alkali metal hydroxide in close to the stoichiometric amount.

It has now been found that the 4-methylmercapto-2-aminobutyramide obtained as an intermediate can be hydrolysed by alkali metal hydroxides without the formation of undesirable by-products such as dipeptides. Solutions of alkali metal methioninate prepared in this way can be directly used in feedstuffs. They may have a concentration, expressed as methionine, of 30 to 60%, and preferably 40 to 45%, by weight, and are free from harmful by-products and inorganic salts.

The process of the invention may be effected by heating 4-methylmercapto-2-aminobutyramide, optionally prepared in situ by the process described in French Patent No. 2,372,797, in an autoclave in an aqueous solution of an alkali metal hydroxide at a temperature of between 100° and 200° C. for 5 to 10 minutes, and then,

after degassing to remove the ammonia formed, cooling the solution obtained, which can be used directly as an additive for feedstuffs.

In general, the amount of alkali metal hydroxide used is between 0.9 and 1.1 mole per mole of amide introduced. Sodium hydroxide is preferably used as the alkali metal hydroxide.

The hydrolysis of the amide can be performed in a dilute medium, and the solution of alkali metal methioninate obtained then brought to the desired concentration of 30 to 60%, preferably 40 to 45%, by removal of water. Preferably, however, the hydrolysis is performed in such a way that the solution of methioninate is obtained directly at the desired concentration, thereby making it possible to avoid the expensive operation of concentrating the solution.

The solution of alkali metal methioninate, preferably sodium methioninate, obtained by the process of the invention is stable, especially down to temperatures which can be as low as -15° to -30° C., depending on their concentration. Moreover, the biological properties of the solutions obtained are equivalent to those of solid methionine.

The examples which follow illustrate the invention.

**EXAMPLE 1**

1 mole of 3-methylmercaptpropionaldehyde (MMPA) and 20 mg of triethylamine are introduced into a 500-cm<sup>3</sup> reactor in which it is possible to work under pressure.

1.05 mole of hydrocyanic acid is introduced at a temperature in the region of 20° C. After 10 minutes' reaction, 5 moles of liquid ammonia are added. The mixture is heated to 60° C. for 30 minutes under a pressure of 11.5 bars with vigorous agitation. On releasing the pressure, the excess ammonia is removed. The reaction mixture contains approximately 0.8 mole of residual ammonia per mole of aminonitrile formed. After the mixture has been cooled to a temperature in the region of 10° C., 350 g of an aqueous solution containing 0.2 mole of acetone and 0.2 mole of sodium hydroxide are introduced. The temperature rises to 20°-25° C. The mixture is heated to 30° C. for 1 hour. The excess ammonia and acetone are removed under reduced pressure. 68 g of 50% caustic soda solution (0.85 mole) are then added and the mixture is heated to 180° C. for 5 minutes. The pressure is 19 bars. The pressure is then reduced to atmospheric pressure, and the temperature falls to about 95° C. After the mixture has cooled to a temperature in the region of 20° C., 333 g of a yellow solution containing 43.40% by weight of methionine and 0.055% of weight of ammonia are obtained.

The yield of methionine is 37% with respect to the MMPA introduced.

The residual ammonia content can be reduced by concentration under reduced pressure.

Under these conditions, a solution is obtained whose characteristics are as follows:

methionine	43.7% by weight (0.293 mole/100 g)
Na	7.08% (0.308 gram-atom/100 g)
ammonia	0.013%
viscosity	10 centistokes at 30° C.
density	1.195
crystallization point	-23° C.

The following ov-products are assayed by thin layer chromatography:

diketopiperazine	less than 0.01%
hydantoin	less than 0.01%
hydantoic acid	less than 0.01%
ureidobutyramide	less than 0.01%
2,4-diaminobutyric acid	0.5 to 0.6%
3-aminopyrrolidone	less than or equal to 0.01%
hexahydropyrimidine-carboxylic acid	less than or equal to 0.02%
methionine amide	0.02%
L,L-dipeptide	0.1%
D,L-dipeptide	0.1%

### EXAMPLE 2

50 g of water, 88.8 g of 4-methylmercapto-2-aminobutyramide (0.60 mole) and 50.4 g of 50% sodium hydroxide solution (0.63 mole) are introduced into a 500-cm<sup>3</sup> reactor in which it is possible to work under pressure. The mixture is completed by adding water so as to obtain a reaction mixture weighing 220 g. The mixture is heated to 120° C. in the course of 10 minutes, and then maintained at this temperature for 20 minutes with agitation. The ammonia formed is removed on releasing the pressure. The temperature falls to about 95° C. After the mixture has cooled to a temperature in the region of 20° C., 205 g of a pale yellow solution containing 43.2% by weight of methionine are obtained.

The yield is in the region of 99%.

The biological efficiency of the solutions of alkali metal methioninate obtained by the process of the present invention is comparable to that of the methionine customarily used in solid form, as shown by trials showing the effects of these products on the growth of chicks.

The trial is carried out on male chicks for a period of 8 to 28 days. The animals receive one of ten experimental diets derived from the same basic diet containing 0.54% of sulphur-containing amino acids, the composition of which is as follows:

maize	31%
maize starch	28%
soya bean oil cake	24%
gelatin	10%
tallow	3%
mineral salts and vitamins	4%
L-lysine hydrochloride	0.04%
L-tryptophan	0.04%
D,L-isoleucine	0.05%
D,L-leucine	0.08%
crude proteins	23.2%
lysine	1.18%
methionine	0.30%
methionine + cysteine	0.54%
metabolizable energy	3190 kcal/kg

The experimental feedstuffs vary only in respect of the extent of addition of methionine (0; 0.05; 0.10; and 0.25%) and also in respect of the source of this supplementation (solid methionine containing 99% of methionine base, solution of sodium methioninate according to Example 1 assaying 43.7% of methionine base).

Each batch consists of 12 replicates of 6 chicks per cage.

The results obtained are collated in Table I.

TABLE I

SOURCE OF METHIONINE	EXTENT OF SUPPLEMENTATION % (BASE)	CONSUMPTION Kg/ANIMAL	WEIGHT GAIN g/ANIMAL	FOOD CONVERSION
basic diet	0	1.160	609	1.91
D,L-methionine	0.047	1.179	627	1.88
Sodium D,L-methioninate according to Example 1	0.064	1.228	664	1.85
Solid D,L-methionine	0.097	1.237	684	1.81
Sodium D,L-methioninate according to Example 1	0.102	1.234	694	1.78
Solid D,L-methionine	0.235	1.251	740	1.69
Sodium D,L-methioninate according to Example 1	0.228	1.254	751	1.67

In Table II, the results are collated which show the variation in weight gain in terms of the source and the level of methionine consumed.

TABLE II

REGRESSION EQUATION Y + ax + b	NUMBER OF POINTS PER LINE	CORRELATION COEFFICIENT	MOLECULAR EFFICIENCY
Solid D,L-methionine Y = 0.083 × + 586	36	0.74	100
Sodium D,L-methioninate according to Example 1 Y = 0.086 × + 591	36	0.78	104

The comparison of the regression coefficients shows that the biological efficiency is the same for both the products in question.

We claim:

1. Process for preparing a solution of sodium or potassium methioninate having a concentration, expressed as methionine, of 30 to 60% by weight and suitable for direct use as an additive in feeding livestock, which comprises hydrolysing 4-methylmercapto-2-aminobutyronitrile in the presence of hydroxide ions and acetone, removing the acetone, and hydrolysing the 4-methylmercapto-2-aminobutyramide obtained at a temperature of 100° C. to 180° C. with an aqueous solution of sodium or potassium hydroxide in a proportion of 0.9 to 1.1 mole per mole of the said amide, the initial concentration of said 4-methylmercapto-2-aminobutyramide being such that the methionine content of the solution of sodium or potassium methioninate obtained is between 30 and 60% by weight, and removing the ammonia formed, to produce the said solution of sodium or potassium methioninate free from inorganic salts and from unhydrolysed amide.

2. Process according to claim 1 in which the concentration of the solution of sodium and potassium methioninate is 40 to 45% by weight.

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